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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,725	02/28/2005	Hitoshi Okamoto	P26510	8296

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EXAMINER	
HILL, KEVIN KAI	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
04/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/525,725	OKAMOTO ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *February 28, 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Effective March 21, 2008, the Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Kevin K. Hill, Art Unit 1633 whose contact information is provided at the end of this Action.

Detailed Action

In response to the Requirement for Restriction mailed July 3, 2006, Applicant had elected without traverse the invention of Group I, claims 1-8, drawn to vectors containing enhancer sequences from the Islet-1 gene, and cell lines containing said vectors.

Amendments

Applicant's response and amendments, filed January 4, 2008, to the prior Office Action is acknowledged. Applicant has withdrawn Claims 9-13, and amended Claims 1-2 and 4-5.

Claims 9-13 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1-8 are under consideration.

Specification

Sequence compliance

37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application.

1. **The disclosure is objected to for the following reason:** this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences are set forth in the specification that lack sequence identifiers.

The specification is objected to because Figures 14 and 17 contain nucleic acid sequences without a corresponding SEQ ID NO in the figure nor in the figure legend. When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier,("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings. See MPEP §2422.02.

It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 244.02). **If the sequences are already present in the sequence listing, it would be remedial to amend with clear correspondence the Brief Description of the Drawings or specification to include the appropriate sequence identifiers.** Applicants are required to comply with all of the requirements of 37 CFR 1.821 - 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive.

37 CFR 1.821(f) states that in addition to the paper copy required by paragraph (c) of this section and the computer readable form required by paragraph (e) of this section, a statement that the content of the paper and computer readable copies are the same must be submitted with the computer readable form, *e.g.*, a statement that "the information recorded in computer readable form is identical to the written sequence listing."

Note that if the SEQ.txt file was received via EFSWeb and the text file meets the requirements for the paper copy and CRF, no statement is required.

The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Claims 1-8 stand rejected under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The instant claims, construed as discussed herein above, embrace an isolated regulatory element that is capable of enhancing gene expression efficiency in a motor or sensory neuron, wherein the structural characteristics of the claimed regulatory element are essentially unlimited.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

The Guidelines further state, "[s]atisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the Applicant was in possession of the necessary common attributes or features of the genus in view of the species disclosed" (Id. at 1106, column 3).

In the instant case, the application discloses 6 sequences, which, based on the discussion in Examples 1-4 is presumed to be genomic DNA upstream of the 5' upstream genomic neuronal-specific enhancer sequence for the zebrafish, human, mouse, and pufferfish Islet-1 gene. However, there is no demonstration in the disclosure that the sequences set forth as SEQ ID NO: 1-6 as defined by the broad claims 1, 2, 4 and 5 is sufficient to drive transcription in any or all motor or sensory neuronal cells as recited in the claim. Claims 1, 2, 4 and 5 are broad and read on any sequence capable of eliciting the same enhancing capabilities of the SEQ IDs listed in the claims by deletion, substitution or addition of one to thirty nucleotides. Is the limitation directed at limiting the changes to 30 nucleotides, such that only individual nucleotides a changed? Or can multiple regions be deleted, as long as the individual region is no longer than 30 nucleotides? The claimed nucleotide sequences are hundreds of base pairs long. There is no teaching of which thirty base pairs are to be changed, or how to determine which nucleotides should be altered. The deletion or addition or substitution of even a single nucleotide has the potential to disrupt the enhancer function of the claimed SEQ ID NO. Therefore, it is not clear that the claimed alterations of the sequences set forth in the sequence listing in the claims are actually species of the invention.

Even if one is to assume, *arguendo*, that the functional properties recited in the instant claims are inherent to the nucleic acids set forth as SEQ ID NO: 1-6, these species are not

representative of the broad genus claimed because they clearly do not convey the necessary common attributes or features of essentially any nucleic acid having the recited function.

Furthermore, with regard to the "relevant identifying characteristics" of the claimed invention, the specification provides no disclosure of the structural features that define the function recited in the claims. As stated in MPEP 2163(I)(A), a biomolecules sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes. Thus, applications that seek to claim biological molecules having a defined function and broadly divergent structure must disclose a correlation between that function and a corresponding structure. Although example 2 identifies high homology between SEQ ID NO: 1-4 in base pairs 235-560, 204-528, 206-530 and 211-555 respectively there is no evidence that these specific sequences are sufficient to define a genus wherein these sequences comprises a "deletion, substitution or addition of one to thirty nucleotides" is capable of driving transcription in any or all motor or sensory neuronal cells as presently claimed. Therefore, the application also fails to provide the relevant identifying characteristics of the claimed invention.

An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (i.e., it is capable of driving transcription in a neuronal- specific manner) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the Applicant was in possession of the claimed invention because it does not provide adequate written description for the broad class of a nucleotide sequence of SEQ ID NO: 1-6 in which deletion, substitution or addition of one to thirty nucleotides is capable of driving transcription in a motor or sensory neuron beyond the scope of a nucleic acid selected from the group consisting of a nucleic acid consisting of SEQ ID NO: 1-6. Therefore, the claims are properly rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description.

Applicant's Arguments

Applicant argues that:

a) Applicants submit that the specification teaches methods for introducing mutations to the claimed nucleotide sequences, and recommends against introducing mutations to particular regions of the claimed sequences, which enhance gene expression efficiency in motor neurons (see, e.g., page 9, paragraph 4, through page 10, paragraph 1, of the specification).

b) the claims are also expressly directed to sequences, which are "capable of enhancing gene expression efficiency in motor neurons." Thus, the claims exclude mutations which would not be "capable of enhancing gene expression efficiency in motor neurons." Applicants note that the specification clearly describes the common features or areas of homology between SEQ IDs 1-6 (see, e.g., page 10, lines 2-20, in the specification) and their common function.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), while the specification discloses that such subdomains of SEQ ID NO:1, 2, 3and 4, respectively, should be excluded from mutation (pgs 9-10, joining ¶) as argued by Applicant, the instant recitation of claim 2 actually requires deletion, substitution or addition precisely in these preferred subdomains. As noted in the prior Office Action, the limitation of "up to 30 deletions, substitutions or additions" is indefinite because there is no disclosure if these deletions, substitutions or additions are to a single nucleotide, or a region of the original sequence. A single deletion could encompass 98% of the original sequence, which reads on more than 5% of. the bases in the original sequences, yet could ablate enhancer function. Any alteration of "up to 30 deletions, substitutions or additions" to the regions of SEQ ID NO:1-6 could alter the function of the enhancer nucleotides. Applicant has shown no examples of mutagenesis of these regions to suggest that such alterations result in enhancer properties. Thus a claims directed to SEQ ID NO:1-6 in which mutations deletions or substitutions to sequences would still have enhancer function would require a high degree of experimentation.

With respect to b), the substantive issue is that the claims allow for an enormous genus of sequence permutations in those nucleic acid sequences, SEQ ID NO:1-4 and SEQ ID NO:5-6, respectively, disclosed to have a common structure and/or function. However, if a plurality of

nucleotides are allowed to be mutated in SEQ ID NO:1-4 and SEQ ID NO:5-6, then the species within a given SEQ ID NO and between given the recited SEQ ID NO's no longer share a common structure. While the specification discloses a common structural feature suggested as important for the functional property in the wildtype, non-adulterated SEQ ID NO, the specification does not disclose what polymorphic derivatives of the preferred SEQ ID NO subdomains also share a common structure also responsible for the functional property. Thus, it appears that Applicant is claiming an enormous genus of polynucleotides wherein the non-functional embodiments are structurally indistinguishable from possibly functional embodiments.

Conclusion

3. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill, Ph.D./
Examiner, Art Unit 1633

/Q. JANICE LI/
Primary Examiner, Art Unit 1633